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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/480,236	01/10/00	DIGAN M	4-31157A/USN

001095
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HM12/0619

EXAMINER	
EWOLDT,G	
ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/480,236	Applicant(s) Digan et al.
	Examiner G. R. Ewoldt	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 10, 2001*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-7, 9-16, and 19-34* is/are pending in the application.

4a) Of the above, claim(s) *19-28* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 9-16, and 29-34* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide and/or Amino Acid Sequence Disclosures. Specifically, the $(GGGS)_4$ sequence in Figure 1 must be identified in the Description of the Figures by SEQ ID NO:.

2. In view of Applicant's amendment and response, filed 4/10/01, only the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 4 stands rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in Paper No. 6, mailed 11/21/00.

Applicant's arguments, filed 4/10/01, have been fully considered but have not been found persuasive. Applicant argues that the UCHT-1 antibody recognizes an epitope contributed by both the ε and γ chains, as stated in the specification, and that the Pharmingen Technical Data Sheet, 2000 does not state that the UCHT-1 antibody does not bind the γ chain of CD3. However, the specification merely asserts that the UCHT-1 antibody binds both ε and γ chains and indicates that said antibody is available from PharMingen. The PharMingen Technical Data Sheet, 2000 clearly states on the first line "**CD3ε**" and "PURIFIED MOUSE ANTI-HUMAN CD3ε MONOCLONAL ANTIBODY". No where does the Data Sheet teach that the antibody binds CD3γ. Absent any evidence of said CD3γ binding, Applicant's assertions alone of said binding are insufficient to support the claim.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-16 and 29-34 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,103,235 (2000) in view of Thompson et al. (1995) and Kreitman et al. (1995) or U.S. Patent No. 5,489,525 (1996), for the reasons of record set forth in Paper No. 6, mailed 11/21/00.

Applicant's arguments, filed 4/10/01, have been fully considered but have not been found persuasive. Applicant argues that the prior art does not provide:

A) sufficient motivation to combine the references,
B) a reasonable expectation of success, or
C) all the claim limitations.

Regarding A, Applicant argues that neither the individual Thompson et al., nor Kreitman et al. references, nor the '235, nor the '525 patents provides motivation to combine the references. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the instant case, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the teachings of the references to form a superior immunotoxin from a well-known antibody (UCHT-1) and a well-known toxin (PE), particularly in view of the advantages of using PE over DT, as taught by Thompson et al. Further, Applicant's assertion that the Thompson al. reference actually teaches away

from using a PE conjugate is incorrect. The Thompson et al. reference is silent as to PE.

Regarding B, Applicant appears to be arguing against the breadth of the instant claims in arguing that "It is impossible to know *a priori* the efficacy of a specific fusion immunotoxin that uses an sFv as a binding moiety." However, in the instant case, the specific antibody (UCHT-1) of the instant claims is well-known and effective, as is the specific toxin (PE). Thus, the prior art does indeed provide a reasonable expectation of success.

Regarding C, while Applicant states that the prior art must teach or suggest all the claim limitations as the third "basic criteria" for an obviousness type rejection, Applicant does not specifically indicate how the claim limitations have not been met, other than through the lack of motivation and lack of expectation of success arguments. See Examiner's reply to said arguments above.

7. The following are New Grounds for Rejection necessitated by Applicant's amendment, filed 4/09/01.

8. Claims 1-3, and 50 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) "the polypeptide encoded by one <u>or more</u> nucleotide sequences," (claims 31 and 32),

B) "an antibody having a variable region <u>which is at least 99% identical</u> to the variable region of UCHT-1 and is <u>at least 95% as effective on a molar basis in competing with UCHT-1</u>," (claim 33).

Applicant's amendment, filed 4/10/01, asserts that no new matter has been added, however, specific passages in support of the new claims, particularly the percentage limitations and the more than one nucleotide, have not been indicated.

9. Claims 31-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of a polypeptide encoded by one or more nucleotide sequences which hybridize to SEQ ID NO:2. Said hybridizing nucleotide sequences encompass a virtually unlimited number of polynucleotides, only one of which, SEQ ID NO:2, has been disclosed. Likewise, the specification provides an insufficient written description of antibodies having a variable region which is at least 99% identical to the variable region of UCHT-1 and is at least 95% as effective on a molar basis in competing with UCHT-1. No such variants of the UCHT-1 antibody are disclosed in the specification. Given the essentially unlimited number of antibodies encoded by a virtually unlimited number of polynucleotides encompassed by the claims, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

10. No claim is allowed.

11. Reference AQ on the form 1449, filed 4/13/00, has been lined through and has not been considered because it has not been provided. Reference AS is incorrectly titled "Purified Mouse Anti-Human CD3 Monoclonal Antibody for Immunohistochemistry (IHC)". The proper title is "Purified Mouse Anti-Human CD3ε Monoclonal Antibody for Immunohistochemistry (IHC)".

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the

statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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June 14, 2001

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